UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,670	04/02/2004	Wolfgang Geiger	32860-000718/US	9757

30596 7590 01/22/2007
HARNESS, DICKEY & PIERCE, P.L.C.
P.O.BOX 8910
RESTON, VA 20195

EXAMINER	
SCHLIENTZ, LEAH H	
ART UNIT	PAPER NUMBER
1618	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/815,670	GEIGER, WOLFGANG	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-28 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-28 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 02 April 2004 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 4/2/04 and 8/30/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 – 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a particle comprising a membrane enclosing a particle core, the membrane including a plurality of functional elements integrated in a matrix (claim 1). Depending on the concentration of a body substance, the substance accumulates at and passes through the membrane, which is influenceable by an extracorporeal signal provided for actuating a detector element. Additional variables included within the particle include a detector element (claim 1), a reaction region (claim 6), and a portal element (claim 12). The specification does not provide any description of the claimed functional elements, detector element, body substance, reaction region, and portal element required to make and use the particle as broadly claimed by functional language.

The factual inquiries that have been considered include:

- the level of skill and knowledge in the art
- physical and / or chemical structure
- functional characteristics
- the correlation between structure and function
- the method of making
- the representative number of species

The level of skill and knowledge in the art

There are a great number of possible chemical moieties which may function as functional elements, detector elements, reaction regions, and portal elements. There is no description provided regarding which specific chemical moieties are used to represent the particle components and in what combinations with what specific body substances. There is very little predictability in the art concerning any undefined species which may represent a detector element, reaction region, or portal region which may detect, react upon, and/or transport any undefined "body substance." There is no description of which specific type of detector element (i.e. which may be a peptide, receptor for certain types of cells, antibody, etc. for example) would detect a specific body substance from of a vast number of possible moieties which may represent body substances (i.e. which may include various certain types of cells, peptides, proteins, nucleic acids, etc.) that the detector would detect and accumulate in order to yield a useful particle. Furthermore, one of ordinary skill in the art would not know which chemical moiety would represent a reaction region out of an almost unlimited number of chemical species which may be possible. One would not know which specific chemical reaction is supposed to take place in order to achieve substance transformation, as

claimed in claim 6, because there is no description of how the substance is to be transformed and thus one would not know the identity of the reaction region. One would not know the identity of the portal element which is to transport the substance through the matrix, as claimed in claim 12, because one does not know the identity of the substance, and thus there is no description to identify what type of moiety would be compatible with any unknown substance to allow transport of the substance through a matrix.

The physical and/or chemical structure, functional characteristics, and the correlation of structure and function

The specification does not provide any guidance to the specific identity or physical / chemical structure of the variables which represent detector elements, reaction regions, portal elements. Because the structures and physical identities of these elements are undefined, it is unclear how Applicant envisaged suitable elements to satisfy the functional requirements of the particle. Furthermore, there is no description provided to indicate the physical / chemical structure or identity of which specific body substances the various functional elements are to detect, react upon, and/or transport.

The method of making and the representative number of species

There are no steps disclosed which describe a process for actually making the particles. The specification does not describe any embodiments of the specific components to show that applicant envisioned the broad scope of such particles defined only by function.

Because of the wide variety of chemical moieties that may represent "functional elements," including detector elements, reaction regions, and portal elements which are available to the skilled artisan, a more detailed description of what is being claimed is necessary to show possession of the invention. For example, the *specific* physical identity of the functional elements to represent the detector element, reaction region, and portal element should be described in the respective claims, as well as which *specific* body substance the functional elements are to detect, react upon, and/or transport. In sum, the specification does not provide any description of the broad components which represent functional elements (including detector elements, reaction regions, and portal elements) required to make and use the broad particle as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 – 28 are rejected as failing to define the invention in the manner required by 35 U.S.C. 112, second paragraph.

The claim(s) are narrative in form and replete with indefinite and functional or operational language. The structure which goes to make up the device must be clearly and positively specified. The structure must be organized and correlated in such a manner as to present a complete operative device. The "functional elements" of the particle, such as a detector element, reaction region, or portal element, are defined only by function or operation, and the claims are indistinct regarding which chemical moieties would be capable of performing the functions.

Claims 1 – 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the limitation wherein "in dependence on the concentration of a body substance, brings about at least one of substance transport through or substance accumulation at the membrane." The claim is confusing because it is unclear regarding the specific way in which substance transport or substance accumulation at the membrane is dependent upon the concentration of the body substance. For example, there is no indication as to any specific concentration, range of concentration, or even any relative concentration of any specific body substance which may be necessary to achieve the desired result.

Claims 4, 17, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Dependent claims 4, 17, and 20 recite the limitation "wherein release of a drug through the membrane depends on the concentration of the body substance." There is insufficient antecedent basis for this limitation in the claim because the particle of independent claim 1 does not require the presence of a drug therein in order for a drug to be released from the particle membrane.

Claims 6, 19, and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite the limitation "wherein the particle core includes a reaction region intended for substance transformation." The claim is confusing because it is unclear whether the "substance" to be transformed is the same body substance which is transported through or accumulated at the membrane of independent claim 1, or whether the "substance" is a different substance.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 – 3, 5 – 8, 10, 12 – 16, 18, 19, 21 – 24, 26, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Unger (US 5,149,319).

Unger discloses methods for providing localized therapeutic heat to biological tissues and fluids. Gases or gaseous precursors or perfluorocarbons are presented as novel potentiators for ultrasonic hyperthermia. The gas, gaseous precursors, and perfluorocarbons which may be administered into the vasculature (i.e. bloodstream) and are designed to accumulate in cancerous or diseased tissues (abstract). Gaseous precursors can be employed as hyperthermia potentiators (column 2, line 45). The gaseous precursor may be a pH-sensitive gaseous precursor (column 2, line 55) and

are encapsulated in liposomes (column 4, line 10). The liposomes are suitable for intravascular use and range in size from about 30 nm to about 10 microns (column 5, line 14). The liposome membrane is composed of natural or synthetic lipids, including cholesterol, phosphatidylcholine, phosphatidylserine, polymerizable lipids, etc. and may include a synthetic polymer (column 4, lines 45 – 65). It is interpreted that such membrane materials are "attackable" by enzymes in the body because naturally occurring lipids, etc. may be broken down *in vivo*. Incorporated within the liposome membranes are ionophores. The ionophore denotes compounds which facilitate the transport (i.e. acting as a "portal element") of hydrogen ions (i.e. a body substances or endogenous substance) across the liposome membrane to effect a change in pH inside the liposome membrane and include compounds commonly referred to as proton carriers or channel formers. Specific examples of the ionophores include carbonylcyanide, p-trifluoromethoxyphenylhydrazone, etc. (column 5, line 54 – column 6, line 40). The use of ionophores allows liposomes entrapping pH-activated gaseous precursors to efficiently produce a gas (i.e. a reaction or substance transformation at a "reaction region") when exposed to a pH gradient (i.e. a concentration of a body substance, which is H^+). The resulting gas-containing liposomes are capable of being detected by ultrasound imaging (column 8, line 3). The stabilized bubbles, gaseous precursors, and perfluorocarbons accumulate in tumors (i.e. a body substance), and thus the liposomes can be considered "detector elements" because they accumulate at a specific body substance. Ultrasonic energy is transmitted through a tissue, reflected, or absorbed. The potentiators of the invention increase the absorption of sound energy

within the biological tissue, resulting in increased heating and increasing therapeutic effectiveness of ultrasonic hyperthermia (column 8, lines 16 – 20).

Claims 1 – 6, 8 – 11, 14 – 22, and 24 – 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Morrison *et al.* (US 6,099,864).

Morrison discloses microcapsules comprising a polymer shell in which a drug or prodrug and a drug activator can be activated in situ by the application of an external energy source (column 5, lines 60 – 65). The energy may be applied ex vivo, or the microcapsules may be administered to a subject, allowed to reach a desired target, detected at the target site, and then activated by the application of energy. The drug remains inactive in the microcapsule until activated and is released at the desired site of action (column 6, lines 40 – 50). The energy which is applied (i.e. an extracorporeal signal) includes light, an electromagnetic field, sonic, or microwave energy (column 10, lines 63+). The microcapsules are 1 – 20 micron in diameter for optimum intravenous administration (i.e. the bloodstream) (column 9, line 57). The thickness of the coating (i.e. a membrane) of the microcapsules may be 0.01 – 2 microns (column 22, line 30). The coating is preferably a non-phospholipid coating, and the outer membrane may be comprised of hydrophobic such as polyglycerides or hydrophoilic polymers such as PVA (column 26, lines 13 – 21). The microcapsule surface comprise protein, surface charge, etc. on the outer surface (i.e. a detector element) which renders the microcapsules attractive to certain target tissues (cells) (column 22, lines 44 – 52). The type of drug or prodrug encapsulated within the microcapsule may be ergosterol, calciferol, etc. or may

be coencapsulated with an activator (i.e. a reaction region which may transform a substance) (column 7 – 8). The inactive drug becomes activated after the microcapsules have reached the target (i.e. a body substance), and thus the release of the drug is dependent on the presence of a body substance (which is within the scope of concentration because there is no limit regarding specific concentration of a "body substance"). Regarding the method for detecting the particle in claim 15, the microcapsules can co-encapsulate a radio-contrast medium which enables oncologists to monitor the delivery of the anti-tumor microcapsules to target tumors using computerized tomography and radiography that track the distribution of the particles after release from the intra-arterial catheter (column 18, lines 57 – 63).

Conclusions

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

lhs

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER